PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 4-33165A	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/EP2004/003819	International filing date *(day/month/year)* 08.04.2004	Priority date *(day/month/year)* 11.04.2003
International Patent Classification (IPC) or national classification and IPC C07D239/42, C07D403/04, C07D403/10, C07D403/14, C07D409/04, C07D409/14, C07D413/10, A61K31/506, A61P1/00, A61P11/00, A61P17/00, A61P19/00, A61P25/00, A61P35/00, A61P37/00		
Applicant NOVARTIS AG		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
23.10.2004	01.03.2005
Name and mailing address of the international preliminary examining authority: European Patent Office - Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	Authorized Officer Hoepfner, W Telephone No. +49 30 25901-337

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/003819

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:

   ☐ international search (under Rules 12.3 and 23.1(b))
   ☐ publication of the international application (under Rule 12.4)
   ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-205 as originally filed

   Claims, Numbers

   1-11 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 11 (with respect to novelty, inventive step and industrial applicability)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 11

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	3-5
	No:	Claims	1,2,6-10
Inventive step (IS)	Yes:	Claims	3-5
	No:	Claims	1,2,6-10
Industrial applicability (IA)	Yes:	Claims	1-10
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 6-9 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, the International Examination Authority fully concurs with the objection put forward by the International Search Authority and no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

In the present independent claim 11, language such as "as hereinbefore described" introduces obscurity and thus renders the claim unclear within the meaning of Art. 6 IPC, since it refers to the whole content of the description. Moreover, such language interferes with Rule 6.2 a) PCT. Consequently, the International Examination Authority fully concurs with the objection put forward by the International Search Authority and no opinion will be formulated with respect to novelty, inventive step and industrial applicability of the subject-matter of this claim (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

D1: WO 96/40143 A (ADAMS JERRY LEROY ; BOEHM JEFFREY CHARLES (US); GALLAGHER TIMOTHY FRAN) 19 December 1996 (1996-12-19)

D2: WO 03/024971 A (PROCTER & GAMBLE) 27 March 2003 (2003-03-27)

Novelty

The document D1 discloses imidazole derivatives which structurally overlap with the compounds of claim 1 the overlapping portion being R^1=pyrimidinyl substituted with -NHR^a, R^a=heterocyclic, optionally substituted, R^4=phenyl, optionally substituted, R^2=heterocyclylC_{1-10}alkyl. The compounds of D1 are useful in the treatment of diseases such as rheumatoid arthritis, inflammatory bowel disease, cachexia or Alzheimer's disease (see page 4, formula (I); page 35, Scheme VII; page 48, lines 12-19; Examples 7, 11, 13).

The document D2 discloses pyrimidine derivatives which are likewise useful in the treatment of the above mentioned diseases (see page 1, paragraph 3; page 2, formula; page 62, paragraph 2).

In view of this prior art, the International Examining Authority fails to acknowledge novelty for the subject-matter of the present independent claims 1 and 6-10 and the present dependent claim 2.

Inventive step

For any remaining novel subject-matter the document D1 could presumably be regarded as closest prior art, since it likewise addresses compounds useful in the treatment of diseases such as rheumatoid arthritis, inflammatory bowel disease, cachexia or Alzheimer's disease and since its compounds appear to come structurally closer to such novel subject-matter.

The distinguishing feature between such novel subject-matter and D1 would be the presence of piperidine (saturated heterocycle).

In the absence of any evidence for an unexpected technical effect linked such a feature, the objective problem solved by such novel subject-matter would be the provision of further compounds useful in the treatment of diseases such as rheumatoid arthritis, inflammatory bowel disease, cachexia or Alzheimer's disease and a method for their preparation.

However, since the modification of the compounds of D1 by replacing an aromatic system with piperidine as solution to such a very general problem was not suggested by any of the documents on file neither taken alone nor in combination, the presence of inventive activity would have been acknowledged for a claim directed to such a solution.

Formal matters

The disclaimer in claims 1 and 2 is not effective (see paragraph "inventive step" above).

The terms "ester" and "prodrug" lack clarity (see claims 1-4).

The same applies to "(optionally) substituted", "lower" alkyl, "lower" alkoxy and the like (see claims 1-3 and 5)

Although in the present claims 1-3 and 5 terms such as "aryl", "heterocycloalkyl" and the like are clear as such, they introduce obscurity in that they unduly extend the scope of the claimed subject-matter (breadth of the claims).

Industrial applicability

There is no doubt that the subject-matter of the present claims 1-5 and 10 is industrially applicable.

However, for the assessment of the present claims 6-9 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.